UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,776	12/12/2003	Mechthild Rieping	7601/80921	9536

7590 07/25/2006

FITCH, EVEN, TABIN & FLANNERY
SUITE 401L
1801 K STREET, NW
WASHINGTON, DC 20006-1201

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,776	RIEPING, MECHTHILD	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,14-20,22,23 and 25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,14-20,22,23 and 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Claims 11, 14-20, 22-23, and 25-34 are pending in the application.

2. Applicant's amendment to the claims, filed on 5/8/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

3. Applicant's arguments filed on 5/8/2006 in response to the Office action mailed on 12/30/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

4. The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

5. Claim 28 is objected to as being grammatically incorrect in the recitation of "process for the producing an L-amino acid." It is suggested that the phrase be amended to recite, *e.g.,* "process for producing an L-amino acid."

Claim Rejections - 35 USC § 112, Second Paragraph

6. Claims 11, 14-20, 22-23, 25-27, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 11 (claims 14-20, 22-23, 25-27, and 33 dependent therefrom) recites the limitation "the coding sequence of SEQ ID NO:1" in line 3 of part b). There is insufficient antecedent basis for this limitation in the claim. Furthermore, it is unclear as to *the* coding sequence that is intended as being encompassed by "the coding sequence of SEQ ID NO:1." Is this meant to encompass the full coding sequence or a portion thereof? It is suggested that applicant clarify the meaning of the term "the coding sequence of SEQ ID NO:1" by recitation of a specific range of nucleotides of SEQ ID NO:1 that are considered to be "the coding sequence of SEQ ID NO:1."

b. Claim 11 (claims 14-19, 22-23, 25-27, and 33 dependent therefrom) recites the term "increased production of L-threonine," which is a relative term that renders the claim indefinite. The term "increased production of L-threonine" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that applicant clarify to what the "increased production of L-threonine" is being compared.

Claim Rejections - 35 USC § 112, First Paragraph

7. Claims 11, 14-20, 22-23, 25-27, and 33 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" (MPEP 8th Ed., October 2006 Revision at pp. 2100-176 and 2100-183) and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description."

Claim 11 (claims 14-20, 22-23, 25-27, and 33 dependent therefrom) has been amended to recite the limitation of "wherein said modification results in an increased production of L-threonine." The examiner can find no showing of support for this limitation in the instant response and there does not appear to be support for this limitation in the specification as filed. The examiner acknowledges the disclosure of a single representative species of Escherichia bacteria as encompassed by the claims that appears to exhibit increased production of L-threonine, *i.e.,* MG442ΔyjgF. However, this single species fails to provide support for the genus of bacteria as encompassed by the claims, which have any recited modification that results in an increase in L-threonine production. Thus, this limitation is considered to be new matter. Applicant is invited to show support for this limitation in the original application.

8. The written description rejection of claims 17-18 under 35 U.S.C. § 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues *UC v. Eli Lilly*, (43 USPQ2d 1398) is not analogous to this case as the patentability of claims 17-18 "really depends upon the patentability of claim 11." According to applicant, claims 17-18 actually narrow the scope of claim 11 and if the process of claim 11 is patentable, then it would apply to all bacteria having the stated mutation, regardless of whether other genetic modification(s) has/have been made.

Applicant's argument is not found persuasive. The genus of bacteria of claim 11 has been found to satisfy the written description requirement in view of a recitation of a structure-function relationship of the modified *Escherichia* bacterium, *i.e.,* the modification results in an increase in L-threonine production. Further, the genus of modified bacterium of claim 28 has a deletion of the entire *yjgF* open reading frame, which is disclosed in the specification to necessarily result in the function of an increase in L-threonine production (specification at Example 4). However, it is the examiner's position that the specification does not adequately describe the genus of bacteria of claims 17-18. In this case, claims 17-18 require that the *Escherichia* bacterium of claim 11 be further modified to comprise one or more gene products or further modified to inactivate a gene as encompassed by the claims. Applicant would appear to take the position that the genes of claims 17-18 are not essential to the claimed invention. However, contrary to applicant's position, the claimed genes are an essential or critical feature of the claimed invention as they are a necessary component of the recited *Escherichia* bacterium. According to MPEP § 2163, "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature

which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." As noted in the prior Office action and undisputed by applicant, each genus of genes of claim 17 encompasses species that are known in the art and additionally encompasses any mutant and variant thereof. The single disclosed species, *i.e.,* the sequence disclosed in the cited reference, fails to represent the variation within the genus of recited "genes." Also noted in the prior Office action and undisputed by applicant, each genus of genes of claim 18 encompasses species that encode mutant and variant proteins that, *e.g.,* have deletion or insertion of multiple amino acids and maintain or exhibit increased biological activity. Again, the single disclosed species, *i.e.,* the sequence disclosed in the cited reference, fails to represent the variation within the genus of recited "genes." While it is acknowledged that the specification discloses a single representative species of each genus of genes, this single species fails to reflect the variation among the members of the genus. Given the lack of description of a representative number of mutant *Escherichia* bacteria, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

9. The scope of enablement rejection of claims 17-18 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: It is noted that applicant does not separately address each rejection under 35 U.S.C. 112, first paragraph, and applicant's argument appears to primarily address only the written description rejection. However, to the extent applicant's argument may be directed the instant rejection, applicant's argument is addressed below.

Applicant argues claims 17-18 actually narrow the scope of claim 11 and if the process of claim 11 is patentable, then it would apply to all bacteria having the stated mutation, regardless of whether other genetic modification(s) has/have been made.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification, while being enabling for a process using an *Escherichia* bacterium of claim 11, further modified to overexpress a nucleic acid as specifically disclosed at pp. 14-18 of the specification, wherein overexpression of the nucleic acid is achieved by transformation of the *Escherichia* bacterium with an expression vector comprising said nucleic acid, or optionally wherein the *Escherichia* bacterium has a mutation or deletion of an endogenous nucleic acid as disclosed at pp. 18-19 of the specification, wherein the expression of the endogenous nucleic acid and the activity of the polypeptide encoded by the endogenous nucleic acid is eliminated by the mutation or deletion, does not reasonably provide enablement for a process using any *Escherichia* bacterium as encompassed by the claims. While the scope of modified *Escherichia* bacterium of claim 11 is found to be enabled by the specification in view of the recitation of a structure-function relationship, it is the examiner's position that the specification does not enable a skilled artisan to make all modified bacteria of claims

17-18 without requiring undue experimentation. In this case, claims 17-18 require that the *Escherichia* bacterium of claim 11 be further modified to comprise one or more gene products or further modified to inactivate a gene as encompassed by the claims. The examiner maintains for the reasons of record, particularly the reasons set forth in the detailed analysis of the relevant Factors of *In re Wands* as set forth at pp. 10-13 of the Office action mailed on 12/30/2005. This reasoning appears to be undisputed by applicant. Thus, at least for the reasons of record, the scope of modified bacteria as encompassed by claims 17-18 is not fully enabled by the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claim(s) 11, 14-16, 19-20, 22-23, 25, and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volz (*Protein Sci* 8:2428-2437, 1999; cited in the IDS filed on 11/18/2004) in view of Enos-Berlage et al. (*J. Bacteriol* 180:6519-6528, 1998; cited in the IDS filed on 11/18/2004). The claims are drawn to a method for the production of an L-amino acid by culturing an *Escherichia* bacterium and recovering or isolating the L-amino acid; wherein the yjgF open reading frame of the bacterium has

been modified according to claim 11, wherein the modification results in an increased L-threonine production.

Volz teaches an attempt to ascertain the function of *Escherichia coli* yjgF gene product by analysis of its crystal structure (p. 2428, abstract). Volz teaches that "[a]lthough the function of YjgF was not entirely determined, the results suggest a number of experiments to complete that goal" (p. 2428, right column, top). According to Volz, one of those experiments is "determination of the phenotype of an organism (*E. coli*...after deletions of all YjgF paralogs" and that "[p]reliminary results toward this approach with *S. typhimurium* have already been reported (Enos-Berlage et al., 1998)" (p. 2435, left column, top). Volz teaches the sequence of E. coli YjgF (p. 2429). Although suggested by Volz, this reference does not teach an *E. coli* with a deleted yjgF gene, nor does the reference teach the use of such E. coli to produce an L-amino acid.

Enos-Berlage et al., which is cited by Volz, teaches a method of phenotyptic characterization of the *S. typhimurium* YjgF gene product using a ygjF-negative mutant (p. 6519, abstract). The methods involved in this analysis involve batch culturing of the ygjF-negative mutant and preparing a cell lysate for DNA isolation and PCR amplification (p. 6520, right column) or collecting an aliquot of the resulting culture medium (see, *e.g.*, "Stringent response assays" at p. 6521, left column). Enos-Berlage et al. also teaches the sequence of E. coli YjgF (p. 6523, Figure 3).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Volz and Enos-Berlage et al. to make an *E. coli* with deletion of the yjgF gene and phenotypic analysis of the resulting mutant by the method of Enos-

Berlage et al. One would have been motivated to do this because of the teachings of Volz as described above. One would have a reasonable expectation of success for making an *E. coli* with deletion of the yjgF gene and analyzing the resulting mutant by the method of Enos-Berlage et al. because of the results of Enos-Berlage et al. Therefore, claims 11, 14-16, 19-20, 22-23, 25, and 28-34, drawn to the method described above would have been obvious to one of ordinary skill in the art.

The following comments are provided in order to clarify the instant rejection. While the combination of Volz and Enos-Berlage et al. do not specifically teach recovery or isolation of an L-amino acid from the *E. coli* with deletion of the yjgF gene or the culture medium thereof, by isolating a cell free extract of *E. coli* with deletion of the yjgF gene (recovery from bacterium) or isolating an aliquot of the culture of an *E. coli* with deletion of the yjgF gene (recovery from medium), one would necessarily recover or isolate the L-amino acid in accordance with the claims, particularly as the claims allow for "constituents of the fermentation broth and/or the biomass in its entirety or portions thereof [to] remain with the isolated L-amino acid" (see claim 16). Also, while the combination of references fails to teach the production of the recited amino acids, in accordance with the evidence provided in the specification, this would be an inherent feature of culturing an *E. coli* with deletion of the yjgF gene.

Conclusion

11. Status of the claims:

Claims 11, 14-20, 22-23, and 25-34 are pending.

Claims 11, 14-20, 22-23, and 25-34 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656